Towards an understanding of defecation disorders: pathophysiology, epidemiology, and clinical implications

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Chapter 1
General introduction and aims of the thesis

Defecation disorders cover a wide range of symptoms, such as fecal incontinence (FI), constipation, or irritable bowel syndrome (IBS) (1, 2) (Table 1). Defecation disorders decrease the quality of life and increase the health care costs (3-5). Unfortunately, our knowledge regarding factors underlying defecation disorders is incomplete, which hampers diagnosis and treatment optimization. Research presented in this thesis adds to the knowledge on anorectal pathophysiology and factors underlying fecal incontinence and constipation, contributing to better treatment of fecal incontinence and constipation.

Table 1. Rome IV criteria for diagnosis of defecation disorders

Defecation disorders	Fecal incontinence	Constipation	Irritable bowel syndrome
Diagnosis criteria	1. Recurrent uncontrolled passage of fecal material in an individual with a developmental age of at least 4 years 2. Criteria fulfilled for the last 3 months. For research studies, consider the onset of symptoms for at least 6 months previously with 2–4 episodes of FI over 4 weeks.	1. Must include 2 or more of the following: • Straining during more than one-fourth (25%) of defecations • Lumpy or hard stools (BSFS 1–2) more than one-fourth (25%) of defecations • Sensation of incomplete evacuation more than one-fourth (25%) of defecations • Sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecations • Manual maneuvers to facilitate more than one fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor) • Fewer than 3 spontaneous bowel movements per week 2. Loose stools are rarely present without the use of laxatives 3. Insufficient criteria for irritable bowel syndrome 4. Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.	1. Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria: • Related to defecation • Associated with a change in frequency of stool • Associated with a change in form (appearance) of stool 2. Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Defecation and fecal continence

In healthy subjects, defecation and fecal continence depend on the coordinated cooperation between pelvic floor muscles and the nerve system. Specifically, the afferent and efferent nerves and their receptors located in the anal canal, anal sphincter, rectum, colon, pelvic floor muscles, and also in the abdominal wall muscle need to orchestrate their effort to regulate the defecation process, and to provide fecal continence when the circumstances for defecation are inappropriate (6).

The defecation process begins with the arrival of stool into the rectum. The puborectal muscle will relax when the social condition is suitable for defecation. During this process, the anorectal angle will straighten. The squatting position (7) and “The Thinker” position (8) can help defecation by straightening the anorectal angle in comparison to the normal sitting position. At the same time, the abdominal muscle contracts to increase the abdominal

pressure, moving the stool along the sigmoid downward to the rectum and further downward to pass the anorectal angle.

When stool distends the rectum, the recto-anal inhibitory reflex, a sampling reflex, is activated, which results in the relaxation of the internal anal sphincter. Consequently, the anal sphincter pressure decreases, which enables the stool to enter the anal canal (9). The rectum will contract during this process and increase the pressure in the rectum to help pass the stools to the anal canal; this process is called the anorectal defecation reflex (10). However, this mechanism can be overruled by voluntary and involuntary fecal continence mechanisms involving contractions of the puborectal muscle and the internal and external anal sphincter. Mechanisms, directly and indirectly, contributing to fecal continence are broadly described and discussed in the next chapter of this thesis (conditionally accepted).

Fecal incontinence

Fecal incontinence is an accidental loss of stool, with a prevalence of 1.4% - 19.5% in different countries (11), and 7.9% in the Netherlands (12). Patients can experience different types of fecal incontinence, depending on the consistency and amount of the lost feces (e.g., solid stool incontinence, liquid incontinence) or the moment of incontinence (for instance, urge incontinence) (13). Incontinence for flatus is considered to be the mildest form of incontinence. Depending on the incontinence severity, patients often undertake various lifestyle alterations, such as wearing a pad, reducing their social activities, or even isolating themselves (14). The severity of fecal incontinence can be evaluated in different ways, where the symptoms-based Wexner incontinence score belongs to one of the most common tools (Table 2). The Wexner score ranges between 0 – 20, where 0 indicates complete continence and 20 is the most severe form of incontinence (14).

Table 2. Wexner incontinence score

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Patients with urge incontinence can sense the stools when the stool is coming but cannot hold the stool until getting to the toilet (13). Urge incontinence may result from decreased rectal capacity or pudendal neuropathy leading to damaged sphincter function (13). Pudendal nerve damage can develop from neurological diseases or traumatic neuropathy from long-duration stretching. The traumatic neuropathy can occur in patients with a long-duration dyssynergic

defecation as these patients strain hard during defecation (15-17). Because the pudendal nerve innervates the external anal sphincter and puborectal muscle (18, 19), and is involved in the voluntary contraction of the anal sphincter, pudendal neuropathy thus negatively influences the motor innervation of the anal sphincter. This, in turn, alters the voluntary contractability of the sphincter and, in this way, leads to urge fecal incontinence (20). If pudendal neuropathy is severe but not complete, the sensory innervation still functions. Therefore, patients feel the accident coming but cannot prevent it by squeezing their anal sphincter.

Of note, fecal incontinence can co-occur with constipation (15, 16, 21-23) and irritable bowel syndrome (IBS)(24)(9). In the first case, chronic constipation can lead to the so-called overflow fecal incontinence with impacted stool accumulated in the proximal bowel; chronic constipation can also result in urge fecal incontinence secondary to the pudendal nerve damage or fecal incontinence secondary to prolapsed hemorrhoids (20, 25). In the second case, i.e., in patients with IBS, the mechanism linking its presence with fecal incontinence is unclear. Patients with IBS and constipation (IBS-C type), dyssynergic defecation, and impacted hard stool in the proximal bowel direction might have fecal overflow incontinence. In the case of patients experiencing IBS and diarrhea (IBS-D type), patients might experience liquid stool incontinence due to chronic diarrhea (24). Besides, the oversensitive rectum in IBS could lead to urge incontinence. This is because when feces enter an overactive rectum, the rectal pressure may quickly increase due to rectal contraction. Despite the importance of IBS in fecal incontinence, the prevalence of FI in each IBS subtype and their symptom characteristics are not clear yet.

Fecal incontinence is manifested by different symptoms and can be underlaid by various factors, including neurological impairments, constipation, or irritable bowel syndrome. Despite this, the current treatment of fecal incontinence is still focused on the incontinence symptom itself instead of considering the underlying causes. This significantly hampers treatment efficacy.

Constipation and dyssynergic defecation

Despite nature equipping us with a sophisticated defecation mechanism, approximately 8.2% - 19% of people still experience problems with defecation, i.e., constipation in the world (26-28), with the incidence being 24.5% in the Netherlands (12).

Currently, hard stool and decreased defecation frequency are frequently considered by doctors to demonstrate constipation. Rome IV criteria for functional constipation take more symptoms into account, including dyssynergic defecation-associated symptoms, such as straining, incomplete defecation, defecation blockage, and manual defecation (2). Even though Rome IV criteria are comprehensive in recognizing symptoms of constipation, they cannot be used to diagnose the underlying causes. Analogically to fecal incontinence, to optimally treat defecation problems and improve the treatment's long-term outcome, it is

crucial to treat not only constipation symptoms but also the cause of constipation. This can be challenging, as there can be various causes of constipation, such as dyssynergic defecation and slow colonic transit constipation (29).

One of the most common causes of constipation is dyssynergic defecation, demonstrated by the unsynchronized use of pelvic floor muscles, and dyssynergic defecation plays a vital role in constipation formation. Rao et al. proposed four subtypes of dyssynergic defecation Veld (30) (Figure 1) based on the measurement with anorectal manometry.

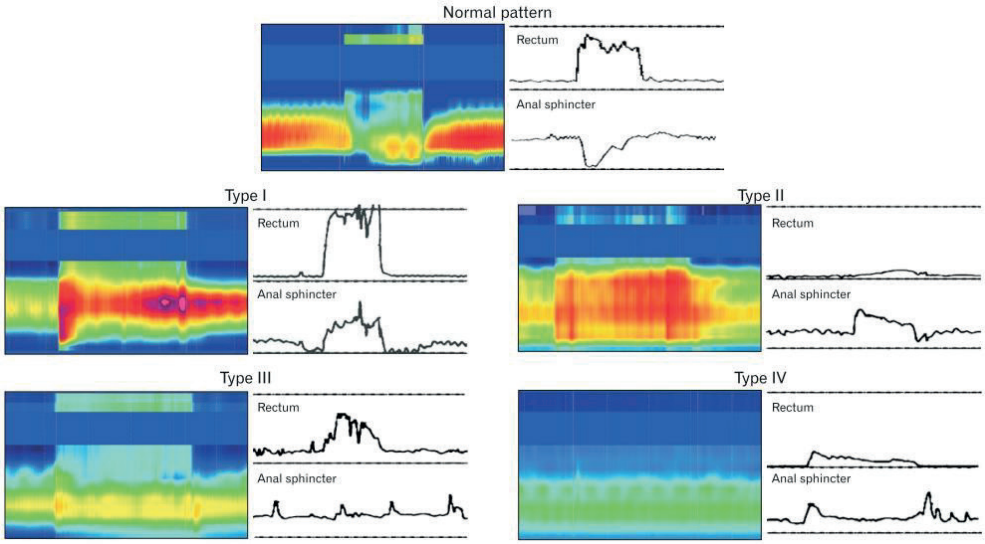

Figure 1. The classification of dyssynergic defecation. Adapted from Rao, S. S. and T. Patcharatrakul (2016). "Diagnosis and treatment of dyssynergic defecation." Journal of Neurogastroenterology and Motility 22(3): 423.

Type I: paradoxical contraction of the anal canal; Type II: inadequate propulsive force and paradoxical anal contraction; Type III: absent or inadequate relaxation of the anal sphincter; Type IV: inadequate propulsive force and absent or inadequate relaxation of the anal sphincter (30).

Overreaction of anal-external sphincter continence reflex (AESCR) (31, 32) can also disable relaxation of the external anal sphincter during defecation and underlay dyssynergic defecation as well.

The severity of general constipation can be evaluated with the Agachan constipation score (range 0 – 30, indicating no constipation and the most severe constipation)(33). The severity of dyssynergic defecation can be evaluated with the Renzi score (range 0 – 20 indicating respectively no symptoms - the highest severity of symptoms) (Table 3) (34).

Table 3. Constipation score systems

Agachan constipation score					
Symptoms/Variables	Scores				
	0	1	2	3	4
Frequency of bowel movements	1-2 times per 1-2 days	1-2 times per week	Once per week	Less than once per week	Less than once per month
History: duration of constipation (years)	0	1-5	5-10	10-20	>20
Difficulty: painful evacuation effort	Never	Rarely	Sometimes	Usually	Always
Completeness: feeling incomplete evacuation	Never	Rarely	Sometimes	Usually	Always
Pain: abdominal pain	Never	Rarely	Sometimes	Usually	Always
Assistance: type of assistance	Without assistance	Stimulative laxatives	Digital assistance or enema	/	/
Time: minutes in lavatory per attempt	<5	5-20	10-20	20-30	>30
Failure: unsuccessful attempts for evacuation per 24 hours	Never	1-3	3-6	6-9	>9
Renzi score					
Symptoms/Variables	Scores				
	0	1	2	3	4
Excessive straining	Never	Rarely	Sometimes	Usually	Always
Incomplete rectal evacuation	Never	Rarely	Sometimes	Usually	Always
Use of enema/laxative	Never	Rarely	Sometimes	Usually	Always
Vaginal/Perineal digital pressure	Never	Rarely	Sometimes	Usually	Always
Abdominal discomfort/pain	Never	Rarely	Sometimes	Usually	Always

To diagnose dyssynergic defecation, only consulting the constipation symptoms is not enough; additional diagnostic tests are required to confirm the symptom-based or anamnesis-based preliminary diagnosis (30). First, anorectal manometry or electromyography (EMG) can

measure anorectal pressures /electricity of the muscle contraction of the anal sphincter generated during defecation to detect dyssynergic defecation patterns. Second, the diagnosis should be supported by a balloon expulsion test, X-ray defecography/dynamic MRI defecography, or markers retention in a colonic transit study (30).

For constipation, lifestyle alteration is the most basic treatment, composed of fiber supplements, increased fluid intake, and regular exercise. Rectal washouts and laxatives are also helpful in improving the effect. In case of slow colonic transit constipation or IBS-constipation, pharmacological treatments have been used, for example, lubiprostone and linaclotide, which promote the intestinal fluid secretion (35, 36); and prucalopride to increase colonic mobility and transit (37). In the case of dyssynergic defecation, botulinum toxin injection was recently proposed to help physiotherapy to relax the contraction of the anal sphincter during defecation (38, 39). But the indication of using botulinum toxin is not clear yet, and some patients do not get good treatment efficacy after botulinum toxin injection (40).

Constipation can also result from organic disorders such as Hirschsprung disease or anorectal malformation (41-45). In the case of Hirschsprung disease, the absence of enteric neurons and glia in the colon prevents relaxation of the distal bowel smooth muscle and, in this way, hampers passage of the stool (46). Moreover, the absence of the recto-anal inhibitory reflex (RAIR) does not allow internal anal sphincter relaxation, which also prevents defecation. The aganglionic bowel segment in Hirschsprung disease can be resected by operation. However, studies on the post-operative long-term outcomes indicate that the prevalence of constipation in already operated HD patients is still relatively high (44). Constipation is also highly prevalent in patients with a congenital anorectal malformation, i.e., after their anal canal was repositioned to the center of the anal sphincter (47). In both groups of patients, dyssynergic defecation is highly prevalent, and this factor should be treated after the organic causes have already been surgically approached (45).

Rectocele and descending perineum correlated with dyssynergic defecation

Timely diagnosis and treatment of constipation in its early stage are crucial. Untreated constipation does not resolve spontaneously but evolutes to more severe forms. Patients with resistant constipation history not reacting to laxatives therapy can be admitted to the hospital to undergo anorectal manometry, during which different physiological factors are brought into the light. Also, a dynamic MR defecography test is frequently used in chronically constipated patients. The last one can often confirm anatomical changes in the pelvic floor, including the existence of rectocele (48) or descending perineum.

From the anatomical point of view, the rectocele is usually an outpunching of the anterior rectum against the posterior vaginal wall commonly seen in female patients with long-term constipation (30). In men, rectoceles are seldom developed because of the anatomical difference in the pelvic floor between males and females (49). Patients with a rectocele can

have various symptoms such as vaginal pressure, defecation blockage, soling, and manual defecation (50).

The rectocele can be diagnosed by collecting patient history, physical examination, or more objectively by measuring with anorectal manometry or dynamic MR defecography alternatively (51).

It has been estimated that the prevalence of rectoceles required operation is around 5% in the female population at 80 years old in America (52, 53). However, this estimation regarding the need for operation is not based on validated criteria. The operation can resect the rectocele and fix the possible rectal or vaginal defect when the conservative treatment does not work (51). Moreover, the operative treatment does not currently yield promising outcomes with high recurrence rates of the rectocele (54-57). The recurrence might result from the fact that the operation corrects the anatomical abnormality, i.e., removes the rectocele, while the pathophysiological mechanism remains untreated. The exact pathophysiological mechanism of rectocele formation is still unknown. Some studies still contribute the mechanism of forming the rectocele to the defect of the rectovaginal septum (50, 58). Some other researchers attributed the formation of the rectocele to chronic constipation and excessive straining during defecation because the rectocele is often accompanied by dyssynergic defecation symptoms (48, 59).

Another common pelvic floor disorder, the descending perineum, is a bulge of the perineum below the normal anatomical position (60). Patients with descending perineum often have a long history of constipation and continuous straining during defecation (61). According to Camilleri et al., the prevalence of descending perineum syndrome is around 8% in all patients with chronic constipation (62).

For the etiology, descending perineum syndrome may be correlated with the pushing to the pelvic floor from the increased intra-abdominal pressure. The intra-abdominal pressure can be increased by contraction of the abdominal wall to push the stools through the high anal canal pressure during the dyssynergic defecation (63). At the same time as the abdominal muscle contraction, the pelvic floor muscle cannot relax normally or even contracts paradoxically in patients with dyssynergic defecation; this further increases the anal canal pressure during straining. This even higher anal sphincter pressure requires further straining of the abdominal muscles to increase the abdominal cavity pressure; thus a “vicious cycle” forms. Then increased intra-abdominal pressure can push the pelvic floor downward during this long-term constipation. Some other studies proposed other factors correlated with descending perineum, such as female gender, birth trauma, old age, and rectocele (64).

Previously, we used x-ray defecography to diagnose the descending perineum. However, x-ray defecography has radiation that limits its wide application (65). Alternatively, we used the dynamic MR defecography in our hospital to avoid ionizing radiation. MR defecography has a higher resolution regarding soft tissues than x-ray defecography (66). However, the value of this new technique in evaluating the descending perineum is still unclear.

Conservative treatment includes laxatives, suppositories, enema, and biofeedback treatment. Whether operation should be applied to descending perineum is still controversial because of the uncertainty of surgical effect (66).

Methods and techniques for diagnosing defecatory problems

Different methods and techniques have been used to diagnose defecatory problems, including symptom-based anamnesis, involving either a face-to-face interview or recently more often incorporated in medical care digital questionnaires (66), and included physical examination such as digital rectal examination (67), anorectal function tests and MRI.

Anorectal function tests

Anorectal manometry and dynamic MR defecography are the two most important measurements for diagnosing defecation disorders. Anorectal manometry can measure the pressure along the level of the anal sphincter, puborectal muscle, and the rectum during rest, squeezing, or defecation. Information regarding voluntary and involuntary contraction can also be provided by manometry. Manometry can also be used with the anal electrical sensory threshold test, which can measure the anal sensation function (68).

MRI

Dynamic MRI defecography is a technique to measure the morphological damage to the anorectum and pelvic floor during different physiological conditions, including rest, squeezing, defecation, and straining. Nowadays, dynamic MRI defecography is recommended by not only colorectal surgeons but also gynecologists and urologists; this is because the organ prolapse in the anterior and middle compartments of the pelvic floor can also be measured in dynamic MR defecography.

In comparison to anorectal manometry, MRI defecography focuses more on the morphological changes of the pelvic floor, such as the anorectal angle, rectocele size, and descending perineum severity. The descending perineum severity can be evaluated (69-75) in dynamic MR defecography using the distance between the anorectal angle and the pubococcygeal line (M line) (76) or the distance between the anorectal angle and the inferior edge of the pubic symphysis (H line) (76). Even though the H and M line lengths are frequently used in patients with pelvic floor disorders (76), the (patho)physiological mechanisms and defecation symptoms underlying these morphological parameters remain unexplored.

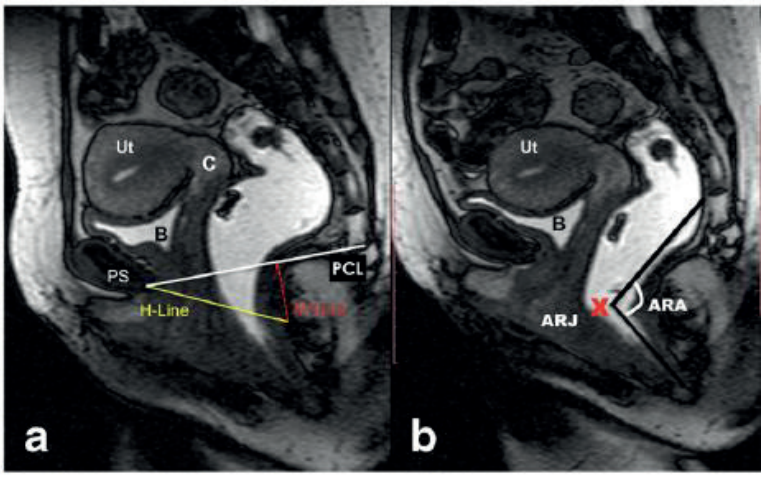

Figure 2. The measurement of the H and M line and the anorectal angle in dynamic MRI defecography. Adapted from El Sayed, R. F., et al. (2017). "Magnetic resonance imaging of pelvic floor dysfunction - joint recommendations of the ESUR and ESGAR Pelvic Floor Working Group." European Radiology 27(5): 2067-2085.

Aims of the thesis

With the research presented in this thesis, we aim to add to the knowledge on the mechanisms, epidemiology, diagnosis, and treatment optimization of defecation disorders. Consequently, the first part of the thesis comprises studies on fundamental mechanisms of defecation disorders. The second part focuses on the symptoms of defecation disorders and the relationship between different kinds of defecation disorders. The last part focuses on looking for innovative diagnoses with dynamic MRI defecography and treatment optimization of botulinum toxin injection for chronic constipation.

Chapter 2, the cornerstone of the present thesis, introduces the physiological mechanism of fecal continence. In this chapter, we will summarize and update the knowledge on possible physiological mechanisms that directly or indirectly regulate fecal continence and reflect on the ambiguous points. This review provides the future direction of research about the mechanism of fecal continence.

In **Chapter 3**, we move from fecal continence to defecation and present our hypothesis and supporting outcomes regarding the role of anal sphincter pressure in the etiology of constipation with rectocele. In this chapter, we try to confirm the association of anal basal pressure just before defecation with rectocele size and constipation severity. This confirmation can justify our policy that constipation, even when presented with mild symptoms, should not be underestimated, and should be treated on time. Chapter 3 aims to add to the knowledge on the etiology of rectocele formation and its recurrence after surgical resection.

Chapters 4, 5, and 6 explore the Chinese population's epidemiological characteristics of defecation disorders. Because the original Groningen Defecation and Fecal Continence questionnaire was till now validated for the Dutch population, we need to first translate and validate it for the Chinese population (**Chapter 4**). Then we aimed to use the online questionnaire to screen the general Chinese population for constipation and investigate the prevalence, risk factors, and clinical characteristics of constipation (**Chapter 5**). In this way, we tried to optimize the current diagnostic procedure for constipation. We would also reflect on the value of the classical method of diagnosing constipation relying on stool consistency and defecation frequency in comparison to dyssynergic defecation-associated symptoms. In **Chapter 6**, we will analyze the co-occurrence of fecal incontinence with irritable bowel syndrome and constipation. Also, the current treatment of fecal incontinence will be investigated and discussed regarding inappropriate treatment focusing on incontinence symptoms. Our study will try to optimize the current treatment of fecal incontinence.

After knowing about the present epidemiological situation of defecation disorders regarding the severity and prevalence, we will investigate the value of the current diagnostic method of defecation disorders. In **Chapter 7,** we will present the value of dynamic MR defecography in evaluating the severity of defecation disorders. The anorectal manometry outcomes will be presented to illustrate the possible physiological changes underlying the anatomical changes.

In **Chapter 8,** we present evidence allowing optimization of constipation treatment using botulinum toxin in paediatric patients. We try to confirm that the injection of botulinum toxin to the anal sphincter aiming to reduce the anal basal pressure is justified in a population of pediatric patients with defecation problems. Additionally, we will evaluate the value of rectal washouts in synergizing the effect of botulinum toxin. This study might contribute to improving treatment efficacy in chronically constipated children.

References

1. Saps M, Velasco-Benitez CA, Langshaw AH, Ramirez-Hernandez CR. Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents: Comparison Between Rome III and Rome IV Criteria. Journal of Pediatrics. 2018;199:212-6.
2. Rome IV criteria [Available from: https://theromefoundation.org/rome-iv/rome-iv-criteria/.
3. Dennison C, Prasad M, Lloyd A, Bhattacharyya SK, Dhawan R, Coyne K. The health-related quality of life and economic burden of constipation. Pharmacoeconomics. 2005;23(5):461-76.
4. Nellesen D, Yee K, Chawla A, Lewis BE, Carson RT. A Systematic Review of the Economic and Humanistic Burden of Illness in Irritable Bowel Syndrome and Chronic Constipation. Journal of Managed Care Pharmacy. 2013;19(9):755-64.
5. Xu X, Menees SB, Zochowski MK, Fenner DE. Economic Cost of Fecal Incontinence. Diseases of the Colon & Rectum. 2012;55(5):586-98.
6. Heitmann PT, Vollebregt PF, Knowles CH, Lunniss PJ, Dinning PG, Scott SM. Understanding the physiology of human defaecation and disorders of continence and evacuation. Nature Reviews Gastroenterology & Hepatology. 2021;18(11):751-69.
7. Sakakibara R, Tsunoyama K, Hosoi H, Takahashi O, Sugiyama M, Kishi M, et al. Influence of Body Position on Defecation in Humans. Luts-Lower Urinary Tract Symptoms. 2010;2(1):16-21.
8. Takano S, Sands D. Influence of body posture on defecation: a prospective study of "The Thinker" position. Techniques in Coloproctology. 2016;20(2):117-21.
9. Broens P, Vanbeckevoort D, Bellon E, Penninckx F. Combined radiologic and manometric study of rectal filling sensation. Diseases of the colon & rectum. 2002;45(8):1016-22.
10. Verkuijl SJ, Trzpis M, Broens PMA. The anorectal defaecation reflex: a prospective intervention study. Colorectal Disease. 2022.
11. Sharma A, Yuan L, Marshall RJ, Merrie AEH, Bissett IP. Systematic review of the prevalence of faecal incontinence. British Journal of Surgery. 2016;103(12):1589-97.
12. Meinds RJ, van Meegdenburg MM, Trzpis M, Broens PMA. On the prevalence of constipation and fecal incontinence, and their co-occurrence, in the Netherlands. International Journal of Colorectal Disease. 2016;32(4):475-83.
13. Rao SSC. Diagnosis and management of fecal incontinence. American Journal of Gastroenterology. 2004;99(8):1585-604.
14. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut. 1999;44(1):77-80.
15. Kiff E, Barnes P, Swash M. Evidence of pudendal neuropathy in patients with perineal descent and chronic straining at stool. Gut. 1984;25(11):1279-82.
16. Snooks SJ, Barnes P, Swash M, Henry M. Damage to the innervation of the pelvic floor musculature in chronic constipation. Gastroenterology. 1985;89(5):977-81.

17. van Meegdenburg MM, Heineman E, Broens PM. Pudendal Neuropathy Alone Results in Urge Incontinence Rather Than in Complete Fecal Incontinence. Dis Colon Rectum. 2015;58(12):1186-93.
18. Guaderrama NM, Liu JM, Nager CW, Pretorius DH, Sheean G, Kassab G, et al. Evidence for the innervation of pelvic floor muscles by the pudendal nerve. Obstetrics and Gynecology. 2005;106(4):774-81.
19. Gagnard C, Godlewski G, Prat D, Lan O, Cousineau J, Maklouf Y. The nerve branches to the external anal sphincter: the macroscopic supply and microscopic structure. Surg Radiol Anat. 1986;8(2):115-9.
20. van Meegdenburg MM, Heineman E, Broens PMA. Pudendal Neuropathy Alone Results in Urge Incontinence Rather Than in Complete Fecal Incontinence. Diseases of the Colon & Rectum. 2015;58(12):1186-93.
21. Read N, Abouzekry L. Why do patients with faecal impaction have faecal incontinence. Gut. 1986;27(3):283-7.
22. Read NW, Abouzekry L, Read MG, Howell P, Ottewell D, Donnelly TC. Anorectal Function in Elderly Patients with Fecal Impaction. Gastroenterology. 1985;89(5):959-66.
23. Scott SM, Lunniss PJ. Risk factors in faecal incontinence. Fecal Incontinence: Springer; 2007. p. 43-66.
24. Simren M, Palsson OS, Heymen S, Bajor A, Tornblom H, Whitehead WE. Fecal incontinence in irritable bowel syndrome: Prevalence and associated factors in Swedish and American patients. Neurogastroenterology and Motility. 2017;29(2).
25. Scarlett Y. Medical management of fecal incontinence. Gastroenterology. 2004;126(1 Suppl 1):S55-63.
26. Chu HK, Zhong LK, Li H, Zhang XJ, Zhang JZ, Hou XH. Epidemiology Characteristics of Constipation for General Population, Pediatric Population, and Elderly Population in China. Gastroenterology Research and Practice. 2014;2014.
27. Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME. Epidemiology of constipation in Europe and Oceania: a systematic review. Bmc Gastroenterology. 2008;8.
28. Higgins PDR, Johanson JE. Epidemiology of constipation in North America: A systematic review. American Journal of Gastroenterology. 2004;99(4):750-9.
29. Mertz H, Naliboff B, Mayer E. Physiology of refractory chronic constipation. Am J Gastroenterol. 1999;94(3):609-15.
30. Rao SS, Patcharatrakul T. Diagnosis and treatment of dyssynergic defecation. Journal of neurogastroenterology and motility. 2016;22(3):423.
31. van Meegdenburg MM, Trzpis M, Heineman E, Broens PM. Increased anal basal pressure in chronic anal fissures may be caused by overreaction of the anal-external sphincter continence reflex. Med Hypotheses. 2016;94:25-9.
32. Trzpis M, Klaase JM, Koop RH, Broens PMA. Fissurectomy combined with botulinum toxin A: a review of short- and long-term efficacy of this treatment strategy for chronic anal fissure; a consecutive proposal of a treatment algorithm for chronic anal fissure. Coloproctology. 2020;42(5):400-8.

33. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum. 1996;39(6):681-5.
34. Renzi A, Brillantino A, Di Sarno G, d'Aniello F. Five-Item Score for Obstructed Defecation Syndrome: Study of Validation. Surgical Innovation. 2013;20(2):119-25.
35. Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. Gut. 2011;60(2):209-18.
36. Ford AC, Moayyedi P, Lacy BE, Lembo AJ, Saito YA, Schiller LR, et al. American College of Gastroenterology Monograph on the Management of Irritable Bowel Syndrome and Chronic Idiopathic Constipation. American Journal of Gastroenterology. 2014;109:S2-S26.
37. Shin A, Camilleri M, Kolar G, Erwin P, West CP, Murad MH. Systematic review with meta-analysis: highly selective 5-HT4 agonists (prucalopride, velusetrag or naronapride) in chronic constipation. Aliment Pharmacol Ther. 2014;39(3):239-53.
38. Hallan R, Melling J, Womack N, Williams N, Waldron D, Morrison J. Treatment of anismus in intractable constipation with botulinum A toxin. The Lancet. 1988;332(8613):714-7.
39. Dressler D, Saberi FA. Botulinum toxin: mechanisms of action. European neurology. 2005;53(1):3-9.
40. Roorda D, Abeln ZA, Oosterlaan J, van Heurn LW, Derikx JP. Botulinum toxin injections after surgery for Hirschsprung disease: Systematic review and meta-analysis. World Journal of Gastroenterology. 2019;25(25):3268.
41. Rubin G, Dale A. Clinical Review:Chronic constipation in children. BMJ. 2006;333(7577):1051-5.
42. Keshtgar AS, Ward HC, Sanei A, Clayden GS. Botulinum toxin, a new treatment modality for chronic idiopathic constipation in children: long-term follow-up of a double-blind randomized trial. Journal of pediatric surgery. 2007;42(4):672-80.
43. Basson S, Charlesworth P, Healy C, Phelps S, Cleeve S. Botulinum toxin use in paediatric colorectal surgery. Pediatric Surgery International. 2014;30(8):833-8.
44. Langer JC. Persistent obstructive symptoms after surgery for Hirschsprung's disease: development of a diagnostic and therapeutic algorithm. J Pediatr Surg. 2004;39(10):1458-62.
45. Meinds RJ, Eggink MC, Heineman E, Broens PMA. Dyssynergic defecation may play an important role in postoperative Hirschsprung's disease patients with severe persistent constipation Analysis of a case series. Journal of Pediatric Surgery. 2014;49(10):1488-92.
46. Heuckeroth RO. Hirschsprung disease - integrating basic science and clinical medicine to improve outcomes. Nature Reviews Gastroenterology & Hepatology. 2018;15(3):152-67.
47. Van Meegdenburg MM, Heineman E, Broens PM. Dyssynergic defecation may aggravate constipation: results of mostly pediatric cases with congenital anorectal malformation. The American Journal of Surgery. 2015;210(2):357-64.
48. Felt-Bersma RJ, Tiersma ES, Cuesta MA. Rectal prolapse, rectal intussusception, rectocele, solitary rectal ulcer syndrome, and enterocele. Gastroenterol Clin North Am. 2008;37(3):645-68, ix.

49. Grossi U, Heinrich H, Di Tanna GL, Taylor SA, Vollebregt PF, Knowles CH, et al. Systematic Characterization of Defecographic Abnormalities in a Consecutive Series of 827 Patients With Chronic Constipation. Diseases of the Colon & Rectum. 2021;64(11):1385-97.
50. Beck DE, Allen NL. Rectocele. Clinics in colon and rectal surgery. 2010;23(2):90.
51. Mustain WC. Functional Disorders: Rectocele. Clinics in Colon and Rectal Surgery. 2017;30(1):63-75.
52. Fialkow MF, Newton KM, Lentz GM, Weiss NS. Lifetime risk of surgical management for pelvic organ prolapse or urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(3):437-40.
53. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 1997;89(4):501-6.
54. Nussler E, Granasen G, Nussler EK, Bixo M, Lofgren M. Repair of recurrent rectocele with posterior colporrhaphy or non-absorbable polypropylene mesh-patient-reported outcomes at 1-year follow-up. International Urogynecology Journal. 2019;30(10):1679-87.
55. Maher C, Baessler K. Surgical management of posterior vaginal wall prolapse: an evidence-based literature review. International Urogynecology Journal. 2006;17(1):84-8.
56. Kahn MA, Stanton SL. Posterior colporrhaphy: Its effects on bowel and sexual function. British Journal of Obstetrics and Gynaecology. 1997;104(1):82-6.
57. Cundiff GW, Fenner D. Evaluation and treatment of women with rectocele: Focus on associated defecatory and sexual dysfunction (vol 104, pg 1403, 2004). Obstetrics and Gynecology. 2005;105(1):222-.
58. Richardson AC. The rectovaginal septum revisited: its relationship to rectocele and its importance in rectocele repair. Clin Obstet Gynecol. 1993;36(4):976-83.
59. Tan C, Geng J, Tang J, Yang X. The relationship between obstructed defecation and true rectocele in patients with pelvic organ prolapse. Scientific Reports. 2020;10(1).
60. Parks AG, Porter NH, Hardcastle J. The syndrome of the descending perineum. Proc R Soc Med. 1966;59(6):477-82.
61. Chaudhry Z, Tarnay C. Descending perineum syndrome: a review of the presentation, diagnosis, and management. International Urogynecology Journal. 2016;27(8):1149-56.
62. Wang XJ, Chedid V, Vijayvargiya P, Camilleri M. Clinical Features and Associations of Descending Perineum Syndrome in 300 Adults with Constipation in Gastroenterology Referral Practice. Digestive Diseases and Sciences. 2020;65(12):3688-95.
63. Saks EK, Harvie HS, Asfaw TS, Arya LA. Clinical significance of obstructive defecatory symptoms in women with pelvic organ prolapse. International Journal of Gynecology & Obstetrics. 2010;111(3):237-40.
64. Chang J, Chung SS. An analysis of factors associated with increased perineal descent in women. J Korean Soc Coloproctol. 2012;28(4):195-200.
65. Goei R, Kemerink G. Radiation dose in defecography. Radiology. 1990;176(1):137-9.
66. Mortele KJ, Fairhurst J. Dynamic MR defecography of the posterior compartment: Indications, techniques and MRI features. European Journal of Radiology. 2007;61(3):462-72.

67. Soh JS, Lee HJ, Jung KW, Yoon IJ, Koo HS, Seo SY, et al. The Diagnostic Value of a Digital Rectal Examination Compared With High-Resolution Anorectal Manometry in Patients With Chronic Constipation and Fecal Incontinence. American Journal of Gastroenterology. 2015;110(8):1197-204.
68. Roe AM, Bartolo DCC, Mortensen NJM. New Method for Assessment of Anal Sensation in Various Anorectal Disorders. British Journal of Surgery. 1986;73(4):310-2.
69. Jorge JM, Habr-Gama A, Wexner SD. Clinical applications and techniques of cinedefecography. Am J Surg. 2001;182(1):93-101.
70. Jorge JMN, Wexner SD, Ehrenpreis ED, Nogueras JJ, Jagelman DG. Does Perineal Descent Correlate with Pudendal Neuropathy. Diseases of the Colon & Rectum. 1993;36(5):475-83.
71. Pucciani F, Boni D, Perna F, Bassotti G, Bellini M. Descending perineum syndrome: are abdominal hysterectomy and bowel habits linked? Dis Colon Rectum. 2005;48(11):2094-9.
72. Choi JS, Wexner SD, Nam YS, Mavrantonis C, Salum MR, Yamaguchi T, et al. Intraobserver and interobserver measurements of the anorectal angle and perineal descent in defecography. Dis Colon Rectum. 2000;43(8):1121-6.
73. Jorge JM, Ger GC, Gonzalez L, Wexner SD. Patient position during cinedefecography. Influence on perineal descent and other measurements. Dis Colon Rectum. 1994;37(9):927-31.
74. Savoye-Collet C, Savoye G, Koning E, Leroi AM, Dacher JN. Defecography in symptomatic older women living at home. Age and Ageing. 2003;32(3):347-50.
75. Boyadzhyan L, Raman SS, Raz S. Role of static and dynamic MR imaging in surgical pelvic floor dysfunction. Radiographics. 2008;28(4):949-67.
76. El Sayed RF, Alt CD, Maccioni F, Meissnitzer M, Masselli G, Manganaro L, et al. Magnetic resonance imaging of pelvic floor dysfunction - joint recommendations of the ESUR and ESGAR Pelvic Floor Working Group. Eur Radiol. 2017;27(5):2067-85.